

WE CLAIM:

5 1. A sustained release oral dosage form for delivering a pharmacologically active agent to the stomach, duodenum, and upper small intestine of a patient with restricted delivery to the lower intestinal tract and colon, the dosage form comprising a therapeutically effective amount of the pharmacologically active agent incorporated in a matrix of at least one biocompatible, hydrophilic polymer that:

10 (a) swells in the presence of water in gastric fluid such that the size of the dosage form is sufficiently increased to provide gastric retention of the dosage form in the stomach of a patient in whom the fed mode has been induced; and

(b) gradually erodes within the gastrointestinal tract over a determinable time period,

15 wherein the ratio of the erosion rate ER obtained *in vitro* for the dosage form using USP disintegration test equipment to the dissolution rate DR obtained *in vitro* for the dosage form using USP dissolution test equipment is in the range of approximately 1.2:1 to approximately 5:1.

20 2. The dosage form of claim 1, wherein the ratio of ER to DR is in the range of approximately 1.2:1 to approximately 3:1.

3. The dosage form of claim 2, wherein the ratio of ER to DR is in the range of approximately 1.3:1 to approximately 2:1.

25 4. The dosage form of claim 3, wherein the ratio of ER to DR is in the range of approximately 1.5:1 to approximately 2:1.

5. The dosage form of claim 1, wherein the therapeutically effective amount of the active agent is in the range of about 0.01% to 80% by volume.

6. The dosage form of claim 1, wherein the therapeutically effective amount of the active agent represents at least 60% of the dosage form by volume.

7. The dosage form of claim 6, wherein the therapeutically effective amount of the active agent represents approximately 60% to 80% of the dosage form by volume.

8. The dosage form of claim 1, wherein following oral administration to a patient in the fed mode, the dosage form is retained in the upper gastrointestinal tract for a time period of about 2 to 12 hours.

9. The dosage form of claim 8, wherein following oral administration to a patient in the fed mode, the dosage form is retained in the upper gastrointestinal tract for a time period of about 4 to 9 hours.

10. The dosage form of claim 8, wherein at least 75 wt.% of the active agent is released within the time period.

11. The dosage form of claim 10, wherein at least 85 wt.% of the active agent is released within the time period.

12. The dosage form of claim 9, wherein at least 75 wt.% of the active agent is released within the time period.

13. The dosage form of claim 12, wherein at least 85 wt.% of the active agent is released within the time period.

14. The dosage form of claim 1, wherein at least 90 wt.% of the dosage form disintegrates *in vitro* in the range of about 1.5 to about 12 hours using USP disintegration test equipment, and at least 90% of the drug is released *in vitro* in less than 25 hours using USP dissolution test equipment.

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15. The dosage form of claim 14, wherein at least 90 wt.% of the dosage form disintegrates *in vitro* in the range of about 1.5 to about 10 hours using USP disintegration test equipment, and at least 90% of the drug is released *in vitro* in less than 20 hours using USP dissolution test equipment.

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16. The dosage form of claim 1, wherein at least 90 wt.% of the dosage form disintegrates *in vitro* in the range of about 1.5 to about 9 hours using USP disintegration test equipment, and at least 90% of the drug is released *in vitro* in less than 16 hours using USP dissolution test equipment.

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17. The dosage form of claim 1, wherein the aqueous solubility of the active agent decreases with increasing pH.

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18. The dosage form of claim 17, wherein the active agent is slightly soluble to soluble in water at a pH in the range of 1 to 4, but becomes substantially insoluble in water at a pH above about 5.

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19. The dosage form of claim 18, wherein the active agent is slightly soluble to soluble in water at a pH in the range of 1 to 2, but becomes substantially insoluble in water at a pH in the range of about 5 to 8.

20. The dosage form of claim 19, wherein the active agent is slightly soluble in water at a pH in the range of 1 to 2, but becomes substantially insoluble in water at a pH in the range of about 5 to 7.5.

5           21. The dosage form of claim 1, wherein the at least one biocompatible hydrophilic polymer is selected from the group consisting of: polyalkylene oxides; cellulosic polymers; acrylic acid and methacrylic acid polymers, and esters thereof; maleic anhydride polymers; polymaleic acid; poly(acrylamides); poly(olefinic alcohol)s; poly(N-vinyl lactams); polyols; polyoxyethylated saccharides; polyoxazolines; polyvinylamines; 10 polyvinylacetates; polyimines; starch and starch-based polymers; polyurethane hydrogels; chitosan; polysaccharide gums; zein; shellac-based polymers; and copolymers and mixtures thereof.

12           22. The dosage form of claim 21, wherein the at least one biocompatible hydrophilic polymer is a polyalkylene oxide polymer or copolymer, a cellulosic polymer, a gum, or a mixture thereof. 15

13           23. The dosage form of claim 22, wherein the at least one biocompatible hydrophilic polymer is a polyalkylene oxide selected from the group consisting of 20 poly(ethylene oxide), poly(ethylene oxide-co-propylene oxide), and mixtures thereof.

14           24. The dosage form of claim 23, wherein the at least one biocompatible hydrophilic polymer is poly(ethylene oxide) optionally in admixture with poly(ethylene oxide-co-propylene oxide). 25

25           25. The dosage form of claim 1, wherein the at least one biocompatible hydrophilic polymer has a number average molecular weight in the range of approximately 5,000 and 20,000,000.

26. The dosage form of claim 1, wherein the active agent is ciprofloxacin or an acid addition salt thereof.

27. The dosage form of claim 26, wherein the active agent is ciprofloxacin  
5 hydrochloride.

28. The dosage form of claim 1, wherein the active agent is a *Helicobacter pylori* eradicator.

10 29. The dosage form of claim 28, wherein said eradicator is selected from the group consisting of bismuth subsalicylate, bismuth citrate, amoxicillin, tetracycline, minocycline, doxycycline, clarithromycin, thiamphenicol, metronidazole, omeprazole, ranitidine, cimetidine, famotidine and combinations thereof.

15 30. The dosage form of claim 29, wherein said eradicator is bismuth subsalicylate.

31. The dosage form of claim 1, wherein the active agent is contained within a vesicle.

20 32. The dosage form of claim 31, wherein the vesicle is selected from the group consisting of liposomes, nanoparticles, proteinoid and amino acid microspheres, and pharmacosomes.

25 33. The dosage form of claim 32, wherein the vesicle is comprised of a nanoparticle.

34. The dosage form of claim 33, wherein the nanoparticle is a nanosphere, a nanocrystal, or a nanocapsule.

35. The dosage form of claim 31, wherein the active agent is water soluble but rendered sparingly water soluble by said vesicle.

36. The dosage form of claim 1, wherein the dosage form is comprised of a tablet.

37. The dosage form of claim 1, wherein the dosage form is comprised of a capsule.

38. A method for delivering a pharmacologically active agent to the upper gastrointestinal tract of a patient over an extended time period while minimizing delivery to the lower gastrointestinal tract and colon, the method comprising orally administering to a patient in whom the fed mode has been induced a sustained release oral dosage form comprised of a therapeutically effective amount of the pharmacologically active agent incorporated in a matrix of at least one biocompatible, hydrophilic polymer that:

(a) swells in the presence of water in gastric fluid such that the size of the dosage form is sufficiently increased to provide gastric retention of the dosage form in the stomach of a patient in whom the fed mode has been induced; and

(b) gradually erodes within the gastrointestinal tract over a determinable time period,

wherein the ratio of the erosion rate ER obtained *in vitro* for the dosage form using USP disintegration test equipment to the dissolution rate DR obtained *in vitro* for the dosage form using USP dissolution test equipment is in the range of approximately 1.2:1 to approximately 5:1.

39. The method of claim 38, wherein following oral administration, the dosage form is retained in the upper gastrointestinal tract for a time period of about 2 to 12 hours.

40. The method of claim 39, wherein following oral administration to a patient in the fed mode, the dosage form is retained in the upper gastrointestinal tract for a time period of about 4 to 9 hours.

5 41. The method of claim 39, wherein at least 75 wt.% of the active agent is released within the time period.

42. The method of claim 41, wherein at least 85 wt.% of the active agent is released within the time period.

10 43. The method of claim 40, wherein at least 75 wt.% of the active agent is released within the time period.

15 44. The method of claim 43, wherein at least 85 wt.% of the active agent is released within the time period.

45. The method of claim 39, wherein the therapeutically effective amount of the active agent is in the range of about 0.01% to 80% by volume.

20 46. The method of claim 45, wherein the therapeutically effective amount of the active agent represents at least 60% of the dosage form by volume.

47. The method of claim 46, wherein the therapeutically effective amount of the active agent represents approximately 60% to 80% of the dosage form by volume.

25 48. The method of claim 39, wherein the active agent is an antibiotic.

49. The method of claim 48, wherein the active agent is selected from the group consisting of ciprofloxacin, minocycline, and acid addition salts thereof.

5 50. The method of claim 49, wherein the active agent is ciprofloxacin.

51. The method of claim 49, wherein the active agent is ciprofloxacin hydrochloride.

10 52. The method of claim 49, wherein the active agent is minocycline.

53. The method of claim 49, wherein the active agent is minocycline hydrochloride.

15 54. The method of claim 39, wherein the active agent is selected from the group consisting of furosemide, gabapentin, losartan, and budesonide.

20 55. A method for treating a human patient suffering from a bacterial infection that is responsive to the oral administration of ciprofloxacin, comprising administering the dosage form of claim 26 to the patient for a therapeutically effective time period.

56. The method of claim 55, wherein the dosage form is administered once daily.

25 57. The method of claim 55, wherein the bacterial infection is infection with mycobacterium avium complex, *Pseudomonas*, *Shigella*, *Salmonella*, toxigenic *E. coli*, *Campylobacter*, *Enterobacter*, or *Bacillus anthracis*



58. A method for selecting an optimized controlled release dosage form for administration to a patient such that the dosage form will have a predetermined drug release profile *in vivo*, the method comprising:

(a) preparing a plurality of different candidate dosage forms each comprised of a biocompatible, hydrophilic polymer and a pharmacologically active agent incorporated therein;

(b) obtaining the erosion rate ER *in vitro* for each candidate dosage form using USP disintegration test equipment;

(c) obtaining the dissolution rate DR *in vitro* for each candidate dosage form using USP dissolution test equipment; and

(d) selecting for administration to a patient that dosage form wherein the ratio of ER to DR is in the range of approximately 1.2:1 to approximately 5:1.

59. The method of claim 58, wherein (d) comprises selecting a dosage form having a ratio of ER to DR is in the range of approximately 1.2:1 to approximately 3:1.

60. The method of claim 59, wherein (d) comprises selecting a dosage form having a ratio of ER to DR is in the range of approximately 1.3:1 to approximately 2:1.

61. The method of claim 60, wherein (d) comprises selecting a dosage form having a ratio of ER to DR is in the range of approximately 1.5:1 to approximately 2:1.